PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC32026A	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IB2004/004287	International filing date *(day/month/year)* 20.12.2004	Priority date *(day/month/year)* 31.12.2003
International Patent Classification (IPC) or national classification and IPC INV. A61K9/16		
Applicant PFIZER PRODUCTS INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.06.2005	24.10.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Ventura Amat, Albert Telephone No. +31 70 340-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/004287

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-47 as originally filed

   Claims, Numbers

   1-26 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has, within the applicable time limit:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest and, where applicable, the protest fee.

   ☐ paid additional fees under protest but the applicable protest fee was not paid.

   ☐ neither restricted the claims nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	23-26
	No:	Claims	1-22
Inventive step (IS)	Yes:	Claims	23-26
	No:	Claims	1-22
Industrial applicability (IA)	Yes:	Claims	1-26
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Re Item IV.

The separate inventions are:

1
A solid composition comprising a plurality of particles comprising a substantially amorphous low solubility drug having a glass transition temperature of at least 50°C and a poloxamer, said drug and said poloxamer together comprising at least 50% of said particles.

2
A solid composition comprising a plurality of particles comprising a substantially amorphous low solubility drug having a Log P value greater than about 6.5 and a poloxamer, said drug and said poloxamer together comprising at least 50% of said particles.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The problem to be solved by the present application is to provide solid compositions that maintain physical stability and enhance the concentration of low solubility drugs when administered to an aqueous environment (Page 1, first paragraph).

The proposed solution is to provide a solid composition comprising a plurality of particles comprising a substantially amorphous low solubility drug having a glass transition temperature of at least 50°C and a poloxamer, said drug and said poloxamer together comprising at least 50% of said particles: This solution is given by the subject matter of claim 1.

A second solution proposed by the Applicant is to provide a solid composition comprising a plurality of particles comprising a substantially amorphous low solubility drug having a Log P value greater than about 6.5 and a poloxamer, said drug and said poloxamer together comprising at least 50% of said particles: This solution is given by the subject matter of claim 2.

The idea to use compositions comprising particles of an amorphous low solubility drug having a glass transition temperature of at least 50°C and poloxamers, said drug and said poloxamer together comprising at least 50% of said particles is not novel, because it is already known from the following prior art document:

- WO 02089835 (Claim 1; examples 4 and 5).

It is therefore known from the prior art , and the idea to use compositions comprising an amorphous low solubility drug and poloxamers could no longer serve as a special technical feature, and therefore as a single general inventive concept.

In the present Application, no further technical feature can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions. Each of the inventions listed below is a distinct invention, characterized by its own technical feature, defining the contribution which each of the claimed inventions considered as a whole, makes over the prior art.

Consequently, there is lack of unity a posteriori and the different inventions not belonging to a common inventive concept are formulated as the different subjects on the communication pursuant to Rule 13 PCT.

The Application has to be divided into the following subjects:

Subject 1): A solid composition comprising a plurality of particles comprising a substantially amorphous low solubility drug having a glass transition temperature of at least 50°C and a poloxamer, said drug and said poloxamer together comprising at least 50% of said particles (claims 1,4-22 partially, 23 entirely, 25, 26 partially).

Subject 2): A solid composition comprising a plurality of particles comprising a substantially amorphous low solubility drug having a Log P value greater than about 6.5 and a poloxamer, said drug and said poloxamer together comprising at least 50% of said particles (claims 2,3 entirely, 4-22 partially, 24 entirely, 25, 26 partially).

Re Item V.

1 Reference is made to the following document:
D1 : WO 02/089835 A (F. HOFFMANN-LA ROCHE) 14 November 2002 (2002-11-14)
D2 : US 20030054042 A1 (ELAINE LIVERSIDGE) 20 March 2003 (2003-03-20)
D3 : WO 03074026 A1 (BIOCOMPATIBLES UK) 12 September 2003 (2003-09-12)

FIRST SUBJECT

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.
Document D1 discloses (Claim 1; examples 4 and 5): A pharmaceutical solid dosage form comprising particles of amorphous nelfinavir mesylate (that has a glass transition temperature of 119°C) and a copolymer of ethylene oxide and propylene oxide (poloxamer 188), the amount of the drug and the polymer together being more of 50% of the particles.

3 INDEPENDENT CLAIM 23

Independent claim 23 is regarded as being novel and inventive.

3.1 NOVELTY

Document D1 discloses (claim 10, examples 4 and 5): A melt process for making solid pharmaceutical forms comprising nelfinavir mesylate and poloxamers. No solvent evaporation method is disclosed.

3.2 INVENTIVE STEP

D1 is regarded as being the closest prior art.

Difference: The method to produce the solid forms of D1 is not a solvent evaporation method.

Problem: To provide an alternative method to produce the solid forms of D1.

Inventive: D1 does not suggest the use of a solvent evaporation method.

4 ARTICLE 6 PCT

4.1 The feature of claim 3, that the drug has a Log P value of higher than about 6.5 and a glass transition temperature of at least 50°C, is not referred to in the description. Claim 3 is therefore not supported by the description as required by Article 6 PCT.

4.2 The feature of claim 4, that the drug has a glass transition temperature of at least 50°C and a Log P value of higher than about 6.5, is not referred to in the description. Claim 4 is therefore not supported by the description as required by Article 6 PCT.

4.3 Claims 17-22 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated function: "In vivo" tests are not repeatable because there are many factors, such as age, individual variability, etc that can not be controlled, thus, the method is not defined. Also the term "control composition consisting essentially of said drug alone" is not defined. The claim at tempts to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

4 DEPENDENT CLAIMS 5,6,9-15

Dependent claims 5,6,9-15 do not contain any features which, in combination with features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article(2) and (3) PCT).

5 DEPENDENT CLAIM 16

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 16 is not new in the sense of Article 33(2) PCT.

As the compositions disclosed in claim 1 are not novel, the properties of these compositions must be shared by the compositions disclosed in D1, and, thus, the properties disclosed in claim 16 can not be novel.

SECOND SUBJECT

2 INDEPENDENT CLAIM 2

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 2 is not new in the sense of Article 33(2) PCT.
Document D2 discloses (Claims 1-3,14,19; page 4, paragraphs 43, 47, 51; examples 2- 5): A pharmaceutical solid dosage form comprising nanoparticles of amorphous rapamycin (that has a log P of 7.76, see WO 03074026 A1, page 21, line 29 to page 23, line 34) and a copolymer of ethylene oxide and propylene oxide (Pluronic F108 or F68), the amount of the drug and the polymer together being more of 50% of the particles.

3 INDEPENDENT CLAIM 24

3.1 D2 is regarded as being the closest prior art.

Difference: In the method to prepare the compositions of D2 the amorphous, low solubility drug having a log P value greater than 6.5 and the poloxamer are mixed in an aqueous solvent but a solution is not formed.

Problem: To provide an alternative method to produce the compositions of D2.

Inventive: D2 does not suggest the formation of a solution comprising the said drug and poloxamer.

4 DEPENDENT CLAIMS 7,8

Dependent claims 7,8 do not contain any features which, in combination with features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article(2) and (3) PCT).